

Antibodies to a Retrovirus Etiologically Associated with Acquired Immunodeficiency Syndrome (AIDS) in Populations with Increased Incidences of the Syndrome

Evidence implicates a retrovirus as the etiologic agent of acquired immunodeficiency syndrome (AIDS). Two prototype isolates have been described. One was isolated from the lymph node cells of a homosexual man with unexplained generalized lymphadenopathy, a syndrome associated with AIDS, and was termed lymphadenopathy-associated virus (LAV) (1). A morphologically similar T-lymphotropic retrovirus (HTLV-III) was isolated from lymphocytes of 26 (36%) of 72 patients with AIDS and from 18 (86%) of 21 patients with conditions thought to be related to AIDS (2). The isolation of retroviruses antigenically identical to LAV from a blood donor-recipient pair, each of whom developed AIDS, provides further evidence that this virus is the etiologic agent of AIDS and may be transmitted through blood transfusion (3).

Although direct comparative results have not been published, HTLV-III and LAV are likely to be the same virus because: they have the same appearance by electron microscopy; they are both lymphotropic and cytopathic for OKT-4 cells; isolates from American AIDS patients, when compared, were immunologically indistinguishable from LAV (3); serologic tests of a large number of specimens from patients with AIDS or related conditions show similar results when either of the prototype viruses is used as antigen (4); and preliminary results suggest that LAV and HTLV-III are at least highly related based on competitive radioimmunoassay of their core proteins (5).

Three basic serologic procedures are currently described for detection of antibody to HTLV-III/LAV: an enzyme-linked immunosorbent assay (ELISA) to whole disrupted virus (6-8); a radioimmunoprecipitation assay (RIPA) to the presumed major core protein (called p25) of LAV (9); and assay of antibody to major viral antigens by the Western blot technique (10, 11). Sera from several high-risk populations are being tested by these techniques by the National Cancer Institute, the Institut Pasteur, and CDC, with the support of numerous collaborators. The objectives of these investigations are to determine the frequency of exposure to HTLV-III/LAV and to correlate seropositivity with current infection, clinical signs and symptoms, and prognosis.

Preliminary data suggest that serologic evidence of exposure to HTLV-III/LAV may be common in certain populations at increased risk for AIDS. Antibody to HTLV-III was detected by ELISA in sera from six (35%) of 17 American homosexual men without symptoms of AIDS (6). Sera from eight (18%) of 44 homosexual men without lymphadenopathy attending a venereal disease clinic in Paris had antibody detected by ELISA to LAV (7). Antibody prevalence to LAV (RIPA) has increased from 1% (1/100) in 1978 to 25% (12/48) in 1980 and 65% (140/215) in 1984 among samples of sera from homosexual men attending a sexually transmitted diseases clinic in San Francisco (12).

Antibody prevalence among the above men tested in 1984 who had no symptoms or clinical signs of AIDS or related conditions was 55% (69/126) (12). In New York City, where the AIDS cases among intravenous (IV) drug users are concentrated, 87% (75/86) of recent heavy IV drug users without AIDS had antibody to LAV by ELISA, while over 58% (50/86) of the same group had antibody to LAV detected by RIPA (13). In contrast, fewer than 10% of 35 methadone patients from New York City had antibody to LAV detected by RIPA. All of these latter patients had been in treatment at least 3 years with greatly reduced IV drug usage (14). Seventy-two percent (18/25) of asymptomatic persons with hemophilia A in a home-care treatment program demonstrated antibody to LAV antigens utilizing the Western blot technique (11). All had used factor VIII concentrates from 1980 to 1982. Reported by DC Des Jarlais, PhD, New York State Div of Substance Abuse Svcs, M Marmor, PhD, H Cohen, MPH, New York University Medical Center, S Yancovitz, MD, J Garber, Beth Israel Medical Center, S Friedman, PhD, Narcotic and Drug Research, MJ Kreek, MD, A Miescher, MD, E Khuri, MD, Rockefeller University, New York City, SM Friedman, MD, New York City Dept of Health, R Rothenberg, MD, State Epidemiologist, New York State Dept of Health; D Echenberg, MD, P O'Malley, E Braff, MD, San Francisco City/County Health Dept, J Chin, MD, State Epidemiologist, California Dept of Health Svcs; P Burtenol, MD, Hemophilia of Georgia, Atlanta, RK Sikes, DVM, State Epidemiologist, Georgia Dept of Human Resources; Div of Viral Diseases, Div of Host Factors, AIDS Activity, Center for Infectious Diseases, CDC.

Editorial Note

Editorial Note: The high prevalence of antibody to HTLV-III/LAV among these groups and the increasing prevalence among homosexual men in San Francisco add further support to HTLV-III/LAV being the etiologic agent of AIDS. They further demonstrate that exposure to the virus is much more common than AIDS itself among populations with increased incidences of the disease. If AIDS follows the pattern of many other infectious diseases, host response to infection would be expected to range from subclinical to severe. Milder disease states for AIDS have been suspected, since the reported frequency of lymphadenopathy and immunologic abnormalities, conditions associated with AIDS, has also been high in these groups. These data, based on limited samples of high-risk groups, suggest the spectrum of response to infection with HTLV-III/LAV may be wide.

These serologic tests are sufficiently sensitive and specific to be of value in estimating the frequency of infection with HTLV-III/LAV in certain populations and for providing important information about the natural history of the disease in such groups. Less clear are the implications of a positive test result for an individual. For some, the result may be a false positive caused by infection with an antigenically related virus or nonspecific test factors. The determination of the frequency and cause of falsely positive tests is essential for proper interpretation of test results, but remains to be established, particularly in populations, such as blood donors who belong to no known AIDS risk groups, where the prevalence of true infection with HTLV-III/LAV is expected to be very low.

A positive test for most individuals in populations at greater risk of acquiring AIDS will probably mean that the individual has been infected at some time with HTLV-III/LAV. Whether the person is currently infected or immune is not known, based on the serologic test alone--HTLV-III/LAV has been isolated in both the presence and absence of antibody--but the frequency of virus in antibody-positive persons is yet to be determined. For seropositive individuals with mild or no signs of disease, including those in whom the virus can be demonstrated, the prognosis remains uncertain. The incubation period for the life-threatening manifestations of AIDS may range from 1 year to more than 4 years (15).

Carefully planned and executed studies will be required to resolve these issues, and to clarify remaining questions about the natural history of AIDS and risk factors for transmission of the virus.

Until the usefulness of positive and negative serologic tests is fully established, all individuals in populations with increased incidences of AIDS, as well as those outside such groups with positive tests, should comply with the March 1983 Public Health Service recommendations for the prevention of AIDS to minimize the transmission of the syndrome (16). Abstention from IV drug usage and reduction of needle-sharing and other use of contaminated needles by IV drug users should also be effective in preventing transmission of the virus and of AIDS. There remains no evidence of transmission of AIDS through casual contact. Prevention measures should stress that transmission has been only through intimate sexual contact, sharing of contaminated needles, or, less frequently, through transfusion of blood or blood products.

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